

Metabolic and electric brain patterns during pleasant and unpleasant emotions induced by music masterpieces

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Abstract

Brain correlates comparing pleasant and unpleasant states induced by three dissimilar masterpiece excerpts were obtained. Related emotional reactions to the music were studied using Principal Component Analysis of validated reports, fMRI, and EEG coherent activity. A piano selection by Bach and a symphonic passage from Mahler widely differing in musical features were used as pleasing pieces. A segment by Prokofiev was used as an unpleasing stimulus. Ten consecutive 30 s segments of each piece alternating with random static noise were played to 19 non-musician volunteers for a total of 30 min of auditory stimulation. Both brain approaches identified a left cortical network involved with pleasant feelings (Bach and Mahler vs. Prokofiev) including the left primary auditory area, posterior temporal, inferior parietal and prefrontal regions. While the primary auditory zone may provide an early affective quality, left cognitive areas may contribute to pleasant feelings when melodic sequences follow expected rules. In contrast, unpleasant emotions (Prokofiev vs. Bach and Mahler) involved the activation of the right frontopolar and paralimbic areas. Left activation with pleasant and right with unpleasant musical feelings is consistent with right supremacy in novel situations and left in predictable processes. When all musical excerpts were jointly compared to noise, in addition to bilateral auditory activation, the left temporal pole, inferior frontal gyrus, and frontopolar area were activated suggesting that cognitive and language processes were recruited in general responses to music. Sensory and cognitive integration seems required for musical emotion.

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1. Introduction

Music is a humanly-produced complex auditory stimulus that is created, desired, and enjoyed mainly because of its powerful effects on emotions, feelings, and mood states (Thayer et al., 1994; Balkwill and Thompson, 1999; Huron, 2001; Baumgartner et al., 2006). Brain responses to experimentally-produced core musical features such as melodic stimuli (Zatorre et al., 1994; Patterson et al., 2002; Gagnon and

Peretz, 2000), tonal information (Zatorre, 2001; Janata et al., 2002), musical timbre (Halpern et al., 2004), or rhythmic structure (Sakai et al., 1999; Samson et al., 2001) have been extensively studied. Since the intricate arrangement of musical features is what evokes an overall affective response (Hevner, 1936; Altenmüller et al., 2002) there has been an increasing interest to use real music as experimental stimulus (Krumhansl, 2003). Indeed, the use of actual music seems not only pertinent but required to study musical emotion. Specifically, music masterpieces are characterized by a skilful handling of various sound resources and musical elements to obtain the expression of an idea that usually evokes defined affective states, and consequently are ideally suited to analyze the neural correlates of the emotional response to music (Ogata, 1995; Blood and Zatorre, 2001; Altenmüller et al., 2002).

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Neural correlates of the emotional reactions to music were not studied until recently. A relatively few brain image studies have shown that some intense musical emotions require limbic and paralimbic networks involving the integration of sensory and cognitive information. Thus, stirring and thrilling feelings produced by favourite musical stimuli increase the blood flow in orbitofrontal cortex, medial subcallosal cingulate, and right frontopolar regions (Blood and Zatorre, 2001). Conversely, unpleasant feelings elicited by dissonant stimuli increase the flow in the right parahippocampal gyrus (Blood et al., 1999). An integration of limbic structures with perceptual and cognitive regions has been reported in non-musicians experiencing pleasant feelings elicited by the passive listening of unfamiliar instrumental music (Brown et al., 2004; Koelsch et al., 2006).

Even though the affective reaction to music engages regions that may explain distinct emotional responses, metabolic brain imaging by itself does not convey information on functional interactions among areas. While functional magnetic resonance imaging (fMRI) provides information on the brain areas involved in the processing of a particular stimulus, some electroencephalographic (EEG) analyses, especially coherent activity, reveal regional and global interactions. Functional coupling or coherent activation among brain sectors has become relevant in the explanation of several attentive, cognitive, and emotional operations. Coherent EEG activity (Singer, 1999; Nunez et al., 2001) related to information processing in specific frequencies (Basar et al., 2001; Patel and Balaban, 2000) may serve as a “binding” mechanism to integrate distant brain processes into unified emotional experiences and an increased coherent activity among cortical areas during musical processing has been reported (Petsche and Etlinger, 1998; Bhattacharya et al., 2001).

Since musical stimuli consist of a temporal flow of organized auditory events, music understanding and concurrent emotions can only be achieved over long time windows, in the order of seconds to minutes. The EEG is not only a suitable method to follow the moment to moment changes induced during prolonged periods of music listening, but also provides a temporal average of brain activity induced by the continuous flow of tones when an epoch of several seconds is analyzed (Bhattacharya et al., 2001; Patel and Balaban, 2000). For example, ongoing electrical activity recorded within the hippocampus changes with dissonant and unsettling musical intervals (Wieser and Mazzola, 1986). Furthermore, Ramos and Corsi-Cabrera (1989) found increased theta and decreased alpha activity using pleasant musical pieces.

In the present study brain correlates of some emotional reactions to music were analyzed in non-musicians during the listening of unfamiliar instrumental masterpieces without the request to perform any cognitive task, except paying attention to the music. In this way, brain resources become more available for spontaneous recollections, impressions, and feelings (Mulholland, 1995). Among the many musical masterpieces that have been carefully tested (Ramos et al., 1996; Flores-Gutiérrez, 2001), three were selected in view of their confirmed affective effects. A piano excerpt by J.S.

Bach and a passage from G. Mahler's 5th Symphony were chosen because consistently elicit pleasant emotions, and a segment by J. Prodromidès because it was reliably reported to engender unpleasant emotions. Since there is no emotionally neutral music (Flores-Gutiérrez, 2001) to be used as control, brain correlates of emotional experience were singled out by comparing the pleasant and unpleasant emotional states reported by the subjects after listening to these music excerpts.

The specific emotions induced by each piece were identified using previously validated scales in 335 subjects (Ramos et al., 1996; Flores-Gutiérrez, 2001). Multiple specific feeling-denoting and formally-confirmed terms were recorded for each musical piece using visual-analogue scales and the respective affective profile was derived from a Principal Component Analysis of the data. The control of music characteristics such as structural features, expressive sequences, and cultural or idiosyncratic norms was accomplished by adding and comparing musical samples sharing an emotional effect but differing in musical features. Thus, the pleasant feelings elicited by the first two very different pieces were compared to each other and to the unpleasant feelings elicited by the third dissonant piece. The strategy of using music pieces widely different in melody, rhythm, harmony, intensity, spectrum, or instruments used, but evoking similar emotional effects constitutes a rigorous control of these fundamental musical variables. Moreover, since none of these pieces is commonly played in popular media and our subjects stated that they did not know them, such strategy provides a further control of the cultural and learned effects.

The pleasant or unpleasant responses to these carefully selected music excerpts were expected to correlate with distinctive images of localized brain metabolic activation and patterns of coherent interactions among brain regions. Music emotion possibly emerges from the initial activation of brain regions directly involved in cortical music perception, and the subsequent activation of independent emotional systems of the sensory modality, aside from coherent cortical activations involved in the extraction of musical meaning. Since there are no combined brain fMRI and coherent EEG studies of emotions during musical masterpiece listening, an open approach was adopted and a complete exploration of all possible brain regions and inter-electrode combinations was undertaken. Even though the general metabolic and coherent EEG responses was explored without *a-priori* defining regions of interest, we expected to find predominant left hemisphere activation with pleasant music emotions and right hemisphere activation with negative musical emotions coupled with distinct limbic and paralimbic involvement. A dissociation of the left and right hemisphere participation during pleasant and unpleasant musical emotions can be expected because positive and negative affects involve predominant activation of the left and right hemisphere respectively (Davidson, 1992; Blood et al., 1999; Herrington et al., 2005; Koelsch et al., 2006). Moreover, using music stimuli, Gagnon and Peretz (2000) found left hemisphere advantage for pleasantness ratings of tonal and atonal melodies, and activations of left fronto-temporal regions with musically elicited positive feelings and of right anterior

brain regions with negative feelings have been reported (Altenmüller et al., 2002; Schmidt and Trainor, 2001).

2. Methods

2.1. Subjects

After being selected from the university community, and giving written informed consent, a total of 19 subjects (11 men and 8 women) with a mean age of 25 years ($SD=3.05$) participated as passive music listeners in the study. Six participated in the fMRI study and 16 in the EEG study. Three subjects underwent both measurements in separate sessions, first the fMRI and then the EEG from 3 to 6 months later. Structured interviews insured that the subjects had no formal music training, were right-handed, in general good health, free from neurological symptoms or psychoactive drugs use, and that women were registered between 5th and 10th day of the menstrual cycle to diminish the effect of hormonal variations (Solis-Ortiz et al., 1994).

2.2. Music and noise stimuli

In accord to the subjective emotions known to be elicited by them, three musical excerpts unknown to the participants were chosen as stimuli. In order to produce pleasant and happy feelings two pieces were used: a soft section for piano, tonal and consonant, in tempo andante (Invention for three parts, BWV 789 by J.S. Bach), and a vigorous, complex, and dramatic composition for symphonic orchestra (first part from second movement, tempo allegro-agitato of 5th Symphony by G. Mahler). In a study performed with 108 students and using a total of 10 different musical parts (Flores-Gutiérrez, 2001), these two pieces were found equally strong for inducing happiness but different for inducing activation. For the induction of unpleasant and reportedly “fearsome” emotions we used an atonal and athematic piece of music written by contemporary composer J. Prodromidès for the film *Danton*, which was previously validated as fear-inducing by 335 subjects (Ramos et al., 1996). The piece by Prodromidès and the music by Mahler elicited equal high levels of activation. Thus, in terms of a previously reported model of the affective system topography (Díaz and Flores-Gutiérrez, 2001) we used musical pieces that produced emotions located in three of the four quadrants formed by the orthogonal intersection of the hedonic valence and activation variables of emotion: pleasure-tranquillity (Bach), pleasure-activation (Mahler), and displeasure-activation (Prodromidès).

2.3. Music excerpt preparation and stimuli presentation

Since the comprehension and affective responses to music require integration over long periods of time, acoustic stimuli were presented in a block design so that each piece was divided in ten consecutive segments of 30 s, alternated with ten segments of 30 s of white noise, for a total of 10 min for each type of music. Thus, within a 10 min section the subjects heard

consecutive excerpts of only one piece alternating with noise. All subjects heard the three pieces (30 min altogether) and their presentation was counterbalanced among the subjects who were explicitly instructed to remain attentively focused on the auditory stimuli as their only task.

The tracks were prepared with a selection from each work, edited as required by means of the Sound Forge 5.0 program. Tracks were recorded on a CD by means of a digital system. The random noise was obtained from radio static and its sound spectrum was homogeneous and constantly flat.

During the fMRI experiments, the music and noise stimuli were delivered inside the scanner by means of pneumatic earphones serving also to mitigate the noise of the machine, which was the same for all conditions. In the case of the EEG recording session, the subjects were comfortably seated in a sound-attenuating chamber under dim light and the tracks were played in two loudspeakers located at 2.1 m from the subjects, who were instructed to maintain their eyes closed.

2.4. Subjective evaluation

The subjects performed the emotional ratings immediately after listening to each musical piece. Thus, the total session lasted approximately 60 min counting the music presentation and questionnaire completion. Three yes/no questions additionally explored whether the subjects *liked* the piece, *would like to hear it again*, and if they *knew it*. In order to evaluate the subjective feelings elicited by each piece, 19 emotion terms validated in previous studies such as *happy, calm, sad, angry, or frightened* (Ramos et al., 1996; Flores-Gutiérrez, 2001) were presented to the subjects using Likert-type scales consisting of a 10 cm horizontal bar representing absence of the feeling at the left and highest grade at the right. The intensity feature of the reported feeling was later evaluated in cm from the 0 point in the left.

Quantitative results from the subjective scales were submitted to Principal Component Analysis (PCA) (Jolliffe, 1986). Component scores of resulting eigenvectors were compared with ANOVAs for repeated measures with the music pieces as the within-subject variable. Post-hoc comparisons with Tukey's *t*-test allowed us to determine differences associated with subjective feelings for each eigenvector.

2.5. fMRI scanning and analysis

All the functional and anatomical imaging sessions were performed on a 1.5 Tesla model v 9.x General Electric LX Magnetic Resonance scanner equipped with 23 mT/m gradients using a standard quadrature headcoil. The subject's head was securely but comfortably fastened in the head holder in order to minimize movements. Functional images were acquired with GE EPI-BOLD pulse sequence with 90° flip angle, TE=60 ms, TR=3000 ms, FOV=256 mm, using a 64×64 matrix, and 4×4×8 mm voxel dimensions. Seven contiguous (zero gap) 8.0 mm thick axial slices were obtained. Image processing was centred at the temporal lobe. In order to obtain a high-resolution reference, structural images were

obtained for each subject using a high-resolution T1 weighted localized exactly over the same seven sections of the functional studies.

All MR data were transferred to an offline workstation using a GE proprietary image format. All images were transferred and saved into SPM2/Analyze format into time-ordered stacks using MRIcro (Rorden, 2000). All these functional time-ordered stacks were loaded into SPM2 (SPM, 2006). All fMRI group statistics were calculated using SPM2, conducted after image registration and alignment were secured using the standard procedures included in SPM (Friston et al., 1994). All functional images were normalized to the EPI standard provided by SPM. Spatial smoothing with a Gaussian kernel of FWHM 8 mm was applied with no low-pass or high-pass filtering. Functional signals were obtained with correlation to boxcar function with convolution to a hemodynamic response function without time derivative correction (Friston et al., 1995). Statistical analysis of fMRI data is based on General Linear Model (GLM) estimated with a classical Restricted Maximum Likelihood (ReML) using an autoregressive AR (1) model with no Volterra interactions, according to SPM manual (SPM, 2006). The relevant regressors were each of the musical pieces and the implicit contrasts calculated were each regressor against cero to detect activated areas in each musical segment, and each contrast against all others to detect the differences. Clusters composed by less than 5 voxels were excluded from analysis. Functional maps were estimated using Family Wise Error (FWE) correction with threshold $p=0.05$. Significance probability maps were computed for each condition into standardized Talairach space (Lancaster et al., 2000).

Brain image correlates of pleasant music feelings were assessed by subtracting the periods of Prodromidès listening from the average of Bach and Mahler pieces and from each piece separately. Unpleasant feelings were evaluated by the opposite procedure. General and emotionally-unspecific music processing was evaluated by subtracting the noise periods from the average of the three music pieces.

2.6. EEG coherent activity register and analysis

EEG activity was recorded at Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2, Fz, Cz and Pz locations of the 10–20 International System referred to ipsilateral earlobes with Grass golden cup electrodes. Four additional electrodes, two for horizontal and two for vertical eye movements (EOG), were referred to the same earlobe, so that the EOG activity of both eyes referred to the same electrode (A1), making eye-movement detection secure and simple.

EEG, EOG activity, and sound tracks signal were amplified using a Neurodata polygraph with filters set at 1 and 70 Hz (-3 dB, roll off -6 dB/oct), digitized at a sampling rate of 512 Hz and stored on a PC using an acquisition program (GRASS-GAMMA, 2005) for the entire duration of the stimuli. The stored EEG was segmented into two-sec epochs synchronized with the start of music or noise tracks. In order to avoid surprise effects, the first and last two-sec epochs of each alternating music and noise epochs were discarded.

The raw recording was visually scrutinized for eye movements, blinks, and muscular artefacts. Rather than correct for eye movements, the more secure strategy of rejecting all 2 sec epochs containing eye movements by directly and simultaneously inspecting the vertical and horizontal eye movement channels was followed. All artefact-free two-sec epochs (at least 465 two-sec epochs for each subject) were analyzed. Correlation spectra for each subject and condition were obtained for 1 Hz bins at 0 time-lag between all pairs of derivations using the program POTENCOR (Guevara et al., 2003). This program initially calculates the Fast Fourier Transform and then determines the correlation spectrum from the autospectra and from the cross-spectrum of the signals proportioning values between -1 and $+1$. The processing of the signals for 0 time-lag was performed according to an equation developed for this purpose. Correlation values were averaged over all epochs of the same condition for each subject and pair of derivations. Before statistical analysis, correlation values were transformed to Fisher's Z scores (Guilford and Fruchter, 1978) to approximate a normal distribution. Lower and higher frequencies (<2 Hz and >25 Hz) were discarded for statistical analysis to avoid eye movements and EMG activity from possible facial muscle contraction due to emotion.

Principal Component Analysis (PCA) was used to reduce the number of variables and obtain independent broad bands based on the actual EEG activity corresponding to the experimental conditions of the study. Absolute power of each frequency bin, derivation, and condition was submitted to PCA followed by varimax rotation. This method extracts orthogonal independent components, in this case frequencies with covariant activity. The procedure has been successfully used to extract broad bands corresponding to particular behavioural states (Corsi-Cabrera et al., 2000; Merica and Fortune, 2005). Only eigenvectors associated with eigenvalues higher than 1 were considered, and factor loadings higher than 0.5 were required to include a frequency bin in a component. The following four bands were extracted: 3–8 Hz, 8–10 Hz, 11–14 Hz, and 14–25 Hz (eigenvalues: 7.57, 5.59, 2.87, and 3.01, explaining 24.29%, 13.10%, 12.48%, and 32.92% of the variance, respectively). The bands obtained correspond to the traditional EEG distinctions which have been confirmed by their reactivity and physiological significance (Niedermeyer, 1998). This procedure allowed interpreting the EEG coherent activity in terms of traditional broad bands. Significant results were obtained mainly in the low and upper alpha band (Klimesch, 1999).

In order to verify that the noise blocks were not significantly different, they were compared with ANOVAs for repeated measures with the three blocks of the same noise as within-subject variables. Since only two isolated differences were found, EEG results were averaged over the three noise blocks for further comparisons. To test the differences among musical pieces ANOVAs for repeated measures with Bach, Prodromidès, Mahler, and the averaged noise as within-subjects variables were done for each electrode combination and narrow band. The noise effects were not considered for *post-hoc*

comparisons but were included in the ANOVA tests to take the variability into account. A significance level of $p < 0.003$ was established after Bonferroni correction for $p < 0.01$. For *post-hoc* comparisons Tukey's Studentized *t*-tests were used.

The representation of the brain surface location of the electrodes used a distribution verified by MRI and superposed by Okamoto et al. (2004) upon a human brain average image (Evans et al., 1993). Even though this allocation does not imply that the activity is generated in the area below the electrode, it does provide for a justified cortical locality relevant for comparison with fMRI activation and the functional interpretation of the results.

3. Results

3.1. Subjective ratings

Table 1 shows the eigenvectors yielded by Principal Component Analysis of the previously selected and validated emotion adjectives, and the percentage of variance explained by each one. Two main eigenvectors emerged from the analysis; the first extracted 8 adjectives associated with *Pleasant* feelings and the second extracted 6 adjectives related with *Unpleasant* feelings. The *attentive* and *involved* adjectives gathered in a third eigenvector. The fourth eigenvector identified the terms *afflicted* and *sad*. Finally, *Activation*-related adjectives were joined in the fifth eigenvector.

Fig. 1 shows the subjective ratings elicited by the three musical excerpts. In agreement with previous results (Ramos

et al., 1996; Flores-Gutiérrez, 2001), the music by Bach and Mahler compared to Prodromidès induces significantly high positive emotions and low negative emotions in the first two eigenvectors. Conversely, Prodromidès elicited more negative and less positive emotions than Bach and Mahler. The fifth *Activation* eigenvector showed significant higher ratings for Mahler than for Bach and Prodromidès. Attention (third eigenvector) was effectively maintained in the music stimulus and did not differ among the pieces. Finally the fourth eigenvector (*Sadness*) did not differ among the pieces.

Answers to specific questions corroborate these findings and verify that the masterpieces were non familiar to the subjects. Thus, a significant number of subjects *liked* the excerpts by Bach and Mahler ($p < 0.01$), found them *pleasant* ($p < 0.01$), and *would like to listen again to them* ($p < 0.05$).

3.2. fMRI and EEG coherent activity results associated with pleasant musical feelings

Predominant activation and increased coherent activity in the left hemisphere were observed with pleasant musical feelings and the pattern differed from the one described below with general musical processing. Thus, pleasant emotions induced by Bach and Mahler as compared to unpleasant ones evoked by Prodromidès activated primary auditory cortex (BA41 and BA42), middle temporal gyrus (BA39), and cuneus (BA19), all in the left hemisphere (Table 2 and Fig. 2A: sample average, C: single subject illustration).

Table 1
Cluster of subjective emotions reported for musical pieces as recognized by Principal Component Analysis

Eigenvectors	1st	2nd	3rd	4th	5th
Emotion adjectives	Pleasant	Unpleasant	Attention	Sadness	Activation
<i>Alegre</i> (cheerful, glad)	0.83*	-0.17	-0.02	-0.32	0.00
<i>Animado</i> (lively, spirited)	0.61*	-0.08	0.16	-0.14	0.57*
<i>Complacido</i> (satisfied, content)	0.73*	-0.31	0.13	0.19	0.04
<i>Confortable</i> (comfortable, placid)	0.76*	-0.13	0.31	0.11	-0.17
<i>Encantado</i> (delighted, charmed)	0.83*	-0.14	0.04	0.01	0.11
<i>Feliz</i> (happy, joyful)	0.86*	-0.08	-0.14	-0.28	-0.02
<i>Inspirado</i> (inspired, exalted)	0.52*	-0.30	0.24	0.5	0.36
<i>Tranquilo</i> (calm, quite)	0.63*	-0.27	0.08	0.02	-0.56*
<i>Asustado</i> (frightened, startled)	-0.43	0.55*	-0.12	0.20	0.36
<i>Enojado</i> (angry, displeased)	-0.09	0.58*	-0.28	0.17	0.16
<i>Fastidiado</i> (annoyed, bothered)	-0.35	0.65*	-0.50	-0.04	0.04
<i>Incómodo</i> (uncomfortable, uneasy)	-0.41	0.61*	-0.40	-0.01	0.11
<i>Inquieto</i> (restless, distressed)	-0.27	0.82*	-0.03	0.16	0.22
<i>Tenso</i> (tense, anxious)	-0.41	0.75*	0.06	0.09	0.28
<i>Atento</i> (attentive, mindful)	0.12	-0.02	0.91*	-0.03	0.03
<i>Involucrado</i> (involved, interested)	-0.04	-0.07	0.81*	0.18	0.25
<i>Afligido</i> (afflicted, grieved)	-0.30	0.43	-0.11	0.66*	-0.05
<i>Triste</i> (sad, sorrowful)	-0.02	0.11	0.13	0.91*	0.00
<i>Excitado</i> (excited, roused)	0.04	0.21	0.20	0.04	0.82*
Eigenvalues	5.1234	4.6588	2.2762	1.9387	1.8897
Variance explained	24.40%	22.19%	10.84%	9.23%	9.00%
<i>p</i> level	0.00001	0.00001	0.004	—	0.0003

Varimax rotated values from Principal Component Analysis, factor loadings higher than 0.5 [*], eigenvalues higher than 1; percentage of the total variance explained by eigenvectors, and *p* level < 0.003 (ANOVAs with music works as the within subjects variable) are shown. Emotion adjectives were provided to subjects in Spanish (italics), the English equivalents are shown in parenthesis.

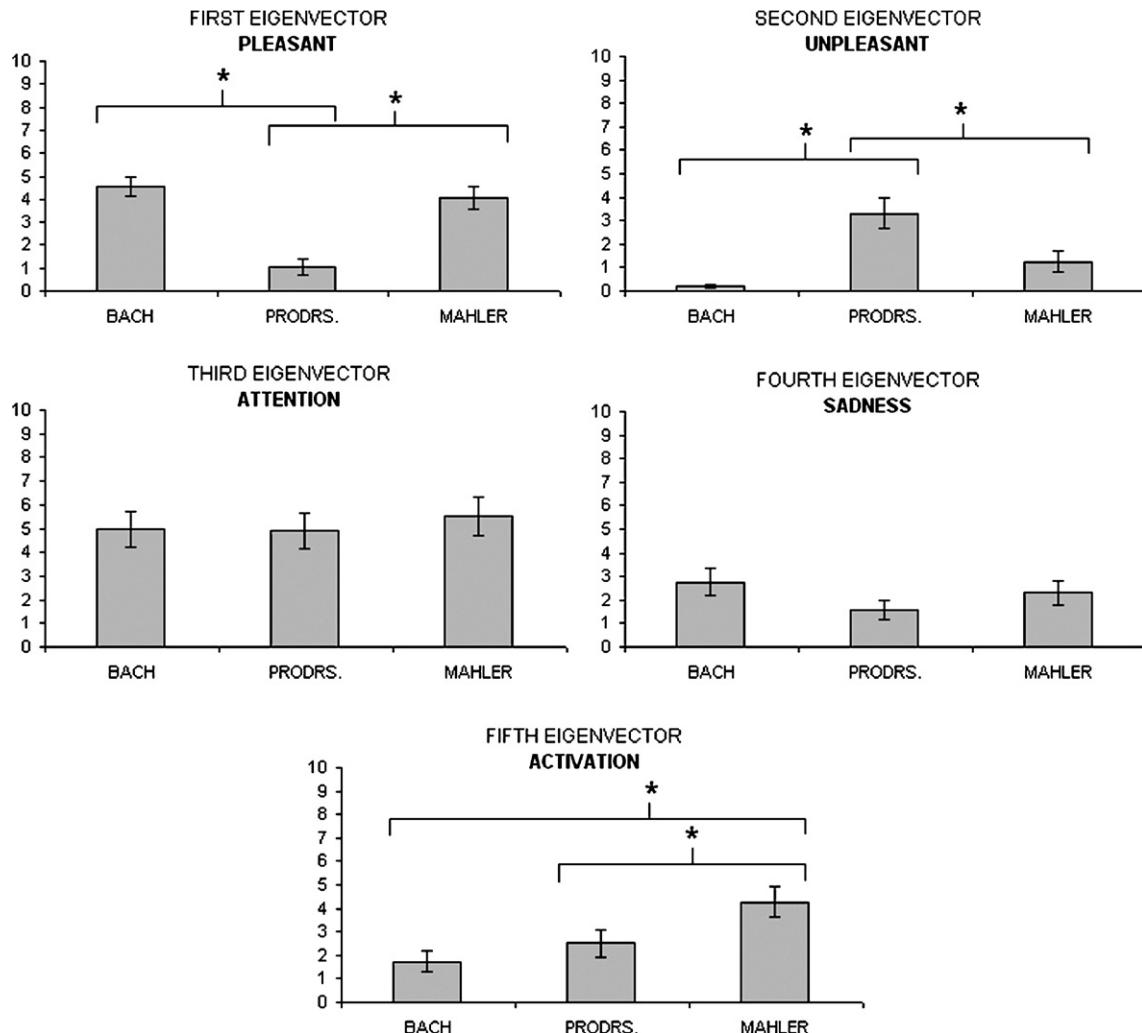


Fig. 1. Principal Component Analysis of subjective emotions reported for the three musical excerpts. Bars represent the mean and standard errors of subjective ratings elicited by the three musical excerpts for the five eigenvectors yielded by Principal Component Analysis. Asterisks and connecting dashed lines indicate significant differences (see Table 1 for corresponding emotion adjectives and eigenvectors).

Additional points of activation (Table 2; not shown in figure), one with pleasant emotions elicited by Bach in left middle frontal gyrus (BA10), and another induced by Mahler in the anterior temporal lobe (BA21), were detected. The right hypothalamus also became active in this latter distinction.

Significant differences associated with subjective pleasant feelings were also observed in EEG coherent activity (Table 3 and Fig. 2B). Pleasant emotions induced by Bach and Mahler as compared to Prodromidès increased coherent activity for two main nodal points, one converging on the T5 electrode and the other in the O1 electrode. Thus, coherent activity was higher with positive than with negative emotions for combinations of the T5 electrode with C3, Cz, Fp1, and Fz at 10 Hz, with T3 at 11 Hz, with F7, C3, Cz and T3 in 13 Hz, and with Cz at 14 Hz. Coherent activity was also higher with positive emotions than with negative emotions between T5 and P3 and Pz electrodes at 10 Hz, with C3, Cz and Pz at 11 Hz, and with F3 and Fz electrodes at 13 Hz. Combinations of the O1 electrode involved higher coherent activity for positive emotions with Cz at 17 Hz, for Bach with

T3 at 11 and 13 Hz, with F3 at 19 Hz, and between O2 with Fz at 13 Hz. (Fig. 2D illustrates the coherent activity similar profile in the averaged 16 subjects on the right and the same subject selected in Fig. 2C on the left).

3.3. fMRI and EEG coherent activity results associated with unpleasant musical feelings

In contrast with pleasant feelings that predominantly implicated the left hemisphere, both fMRI and EEG showed bilateral engagement during unpleasant musical emotions (Table 2). Unpleasant emotions induced by Prodromidès compared to pleasant ones evoked by Bach and Mahler involved a bilateral fMRI activation of the inferior frontal gyrus (BA47) and insula (BA13). The middle (BA11) and inferior frontal gyri (BA44) of the left hemisphere were also activated (Fig. 3A: sample average, C: single subject illustration).

Additional activations (Table 2; not shown in figure) of the orbitofrontal region of the right superior frontal gyrus (BA10)

Table 2
Anatomical location of voxel clusters and statistical significance between conditions

Left	Talairach coord					Right	Talairach coord					
	BA	x	y	z	p		BA	x	y	z	p	
<i>Pleasant</i>												
Bach and Mahler minus Prodromides												
Sup. temporal G	41	-55	-21	3	0.000							
Sup. temporal G	42	-61	-29	7	0.003							
Mid. temporal G	39	-42	-73	22	0.001							
Cuneus	19	-12	-90	30	0.020							
Bach minus Prodromides												
Mid. temporal G	39	-46	-71	20	0.008							
Mid. frontal G	10	-34	54	-9	0.032							
Mahler minus Prodromides												
Mid. temporal G	39	-42	-73	22	0.001	Sub-lobar hypothal.		8	-6	-11	0.006	
Mid. temporal G	21	-55	-21	1	0.001							
Sup. temporal G	42	-61	-29	7	0.001							
Cuneus	19	-12	-90	30	0.027							
<i>Unpleasant</i>												
Prodromides minus Bach and Mahler												
Insula	13	-34	4	9	0.015	Inf. frontal G		47	34	31	-7	0.018
Inf. frontal G	44	-57	12	16	0.018	Insula		13	42	9	16	0.024
Inf. frontal G	47	-38	31	4	0.022							
Mid. frontal G	11	-44	42	-11	0.036							
Prodromides minus Bach												
Mid. temporal G	39	-50	-59	25	0.001	Sup. frontal G		10	26	58	-1	0.019
Prodromides minus Mahler												
Inf. frontal G	45	-57	13	18	0.000	Inf. frontal G		47	34	33	-7	0.000
Inf. frontal G	13	-40	29	4	0.000	Inf. frontal G		13	42	27	4	0.001
Insula	13	-34	6	9	0.000	Insula		13	42	9	16	0.002
Insula	13	-30	16	8	0.024	Insula		13	36	14	12	0.004
Mid. frontal G	11	-44	42	-11	0.004	Sup. temporal G		42	65	-34	18	0.020
Inf. frontal G	47	-40	21	-16	0.006							
Inf. frontal G	45	-50	35	2	0.014							
Mid. temporal G	21	-51	3	-10	0.018							
<i>Activation</i>												
Mahler minus Bach (excitement)												
Inf. frontal G	47	-32	27	-11	0.033	Parahippocampal G		34	24	5	-15	0.000
Parahippocampal G	34	-20	3	-15	0.043	Inf. frontal G		47	30	13	-19	0.000
						Parahippocampal G		37	12	-4	-10	0.000
						Inf. frontal G		47	36	32	-18	0.000
						Sup. frontal G		10	26	58	-1	0.000
						Inf. frontal G		47	46	26	-15	0.015
Bach minus Mahler (calmness)												
Inf. frontal G	13	-42	29	6	0.006	Mid. frontal G		47	34	35	-8	0.000
Inf. frontal G	45	-50	33	6	0.012	Inf. parietal lobule		40	67	-43	24	0.013
Insula	13	-32	16	10	0.034	Inf. Frontal G		45	34	29	6	0.044
Insula	13	-34	6	9	0.038							
Inf. frontal G	45	-57	13	18	0.038							
<i>Music minus noise</i>												
Sup. temporal G	38	-48	15		0.000	Sup. temporal G		22	55	-4	-7	0.000
Inf. frontal G	47	-32	27	-11	0.000	Sup. temporal G		42	63	-21	10	0.000
Sup. temporal G	41	-55	-21	5	0.000	Sub-lobar hypothal.		8	-6	-11	0.033	
Inf. frontal G	9	-44	13	21	0.007							

Ba = Brodmann Area; Talairach coordinates: X = (left [-], right [+]), Y = (posterior [-], anterior [+]), Z = (inferior [-], superior [+]) (Lancaster et al., 2000); Clusters radius = 10 voxels; Family Wise Error corrected $p=0.05$ (Friston et al., 1994).

and left posterior middle temporal gyrus (BA39) were observed with negative emotions (Prodromides) as compared only to Bach. Bilateral activation of the inferior frontal gyrus (BA47) and insula (BA13), right activation of the auditory

area (BA42), and left activation of middle frontal gyrus (BA11) and inferior frontal gyrus (BA45) extending toward BA 47 and BA13 were observed with negative (Prodromides) minus positive emotions induced by Mahler.

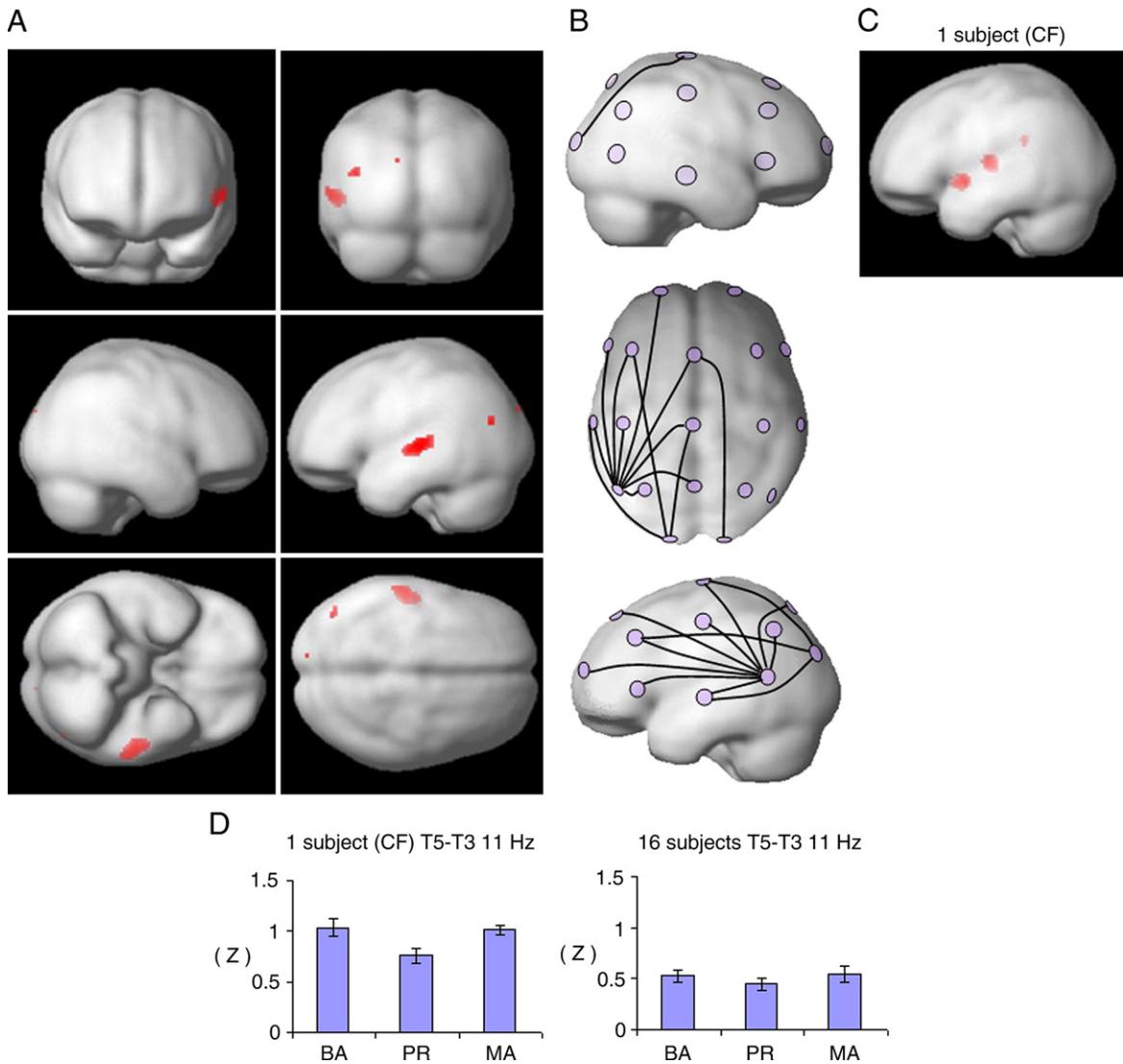


Fig. 2. fMRI and coherent EEG images during pleasant music emotion (Bach and/or Mahler vs. Prodromidès) superimposed on a three-dimensional average brain template. A: Averaged fMRI activations across subjects demonstrating areas in which the activity surpasses the threshold of $p < 0.05$ (corrected). Red colour indicates higher activation sites with pleasant as compared to unpleasant music emotions (see Table 2 for corresponding coordinates and areas). Left column: anterior, right, and inferior views. Right column: posterior, left, and superior views. B: Lines connecting electrodes indicate significantly higher coherent EEG activity with pleasant than unpleasant music (see Table 3 for corresponding frequencies). C: Single subject fMRI illustration of left hemisphere activation. D: EEG correlation profile similarity in full sample (right) and a single subject (left). Brain surface location of the electrodes used the distribution of Okamoto (Okamoto et al., 2004) on the average brain image by Evans (Evans et al., 1993).

An increased EEG coherent activity in unpleasant emotions (Table 3 and Fig. 3) induced by music (Prodromidès compared to Bach and Mahler) was found for combinations of the Fp1 electrode with Cz and Pz for beta frequencies, combinations of the Fp2 electrode with Fz at 11 and 13 Hz, and with C4 in 23 Hz. Coherent activity also increased with negative emotions (Prodromidès) as compared to positive emotions induced by Bach (Fig. 3B) between Fp1 and Fz, between F3 and T3, between F4 with Cz and Fz, and for combinations of the Fp2 electrode with Cz in beta, and with F4 in alpha and beta. Coherent activity was higher with negative (Prodromidès) than with positive emotions elicited by Mahler (Fig. 3B) for Fp2 and F8 in beta. Finally, Fig. 3D illustrates the similar profile in the coherent activity in the

averaged 16 subjects (right) and the same subject selected in 3C (left).

3.4. fMRI and EEG coherent activity results associated with musical excitement or calmness

The reported emotions indicated significant differences between Bach and Mahler that cannot be attributed to hedonic valence, since both were evaluated as similarly pleasant samples. Bach and Mahler excerpts induced different levels of activation-related adjectives so that, while Bach made the subjects feel *calm* or *quiet*, Mahler made them feel *excited* or *roused*. Thus, the main difference between these pieces may be attributed to agitation, rhythm, and tempo conflated in a

Table 3
Coherent activity elicited by different subjective emotional responses to music

Left			Right			Left			Right		
Electrode	Hz	p < 0.003	Electrode	Hz	p < 0.003	Electrode	Hz	p < 0.003	Electrode	Hz	p < 0.003
<i>Pleasant-unpleasant differences</i>											
Bach and Mahler > Prodromides											
O1-Cz	17	0.003				O1-P3	6	0.003	O2-T6	9	0.0006
T5-F7	13	0.00003				O1-Pz	6	0.0009	O2-Cz	10	0.002
T5-C3	10	0.001				T3-C3	13	0.0002	O2-Pz	10	0.003
	13	0.002					15	0.001	O2-T4	9	0.003
T5-Cz	10	0.0001					5	0.002	T4-Fp2	18	0.002
	13	0.002				T3-Cz	15	0.002	T4-C4	22	0.003
T5-Fp1	10	0.0007					13	0.002			
T5-Fz	10	0.0005				T3-Fz	15	0.003			
T5-T3	13	0.0005				T3-P3	14	0.0008			
	11	0.0008				T3-Pz	15	0.001			
Bach > Prodromides						T3-T5	13	0.003			
O1-T3	11	0.0005	O2-Fz	13	0.001						
O1-F3	19	0.001				Noise > music					
T5-C3	11	0.002				C3-F7	12	0.0004	Cz-Fz	12	0.0002
T5-F3	13	0.001				C3-F3	12	0.003	F4-P4	5	0.003
T5-Fz	13	0.0006				C3-Fp1	13	0.003	Fp2-F4	3	0.002
T5-P3	11	0.0009				C3-Fz	12	0.003	Fz-Pz	12	0.003
	10	0.002				F3-O1	25	0.003			
T5-Pz	10	0.0009				F7-Pz	12	0.0004			
	11	0.003				Fp1-C3	12	0.0009			
Prodromides > Bach and Mahler						Fp1-Pz	12	0.0008			
Fp1-Cz	21	0.0003	Fp2-Fz	13	0.0001	Fp1-O1	12	0.003			
Fp1-Pz	21	0.002	Fp2-Fz	11	0.0007						
			Fp2-C4	23	0.001	O1-Fp1	13	0.00007			
Prodromides > Bach						O1-F3	13	0.0009			
Fp1-Fz	18	0.001	F4-Cz	11	0.001	O1-F7	13	0.0001			
			Fp2-Cz	11	0.0007	O1-Fz	13	0.002			
			Fp2-Cz	10	0.003	P3-C3	25	0.0006			
						P3-F7	12	0.0006			
<i>Pleasant activation differences</i>											
Mahler > Bach (excitement)											
Fp1-T3	11	0.0002				P3-F3	25	0.002			
Fp1-T3	15	0.003				P3-Fz	12	0.002			
Bach > Mahler (calmness)											
P3-F3	13	0.001									
P3-F7	13	0.003									
P3-Fz	13	0.002									

Pairs of electrodes and frequencies (Hz) showing significant changes in coherent activity between music stimuli conditions in ANOVAS ($p < 0.003$) and post-hoc comparisons (Tukey's Studentized t -test).

distinct eigenvector called musical “activation” corresponding to the second parameter in the emotion system model (Díaz and Flores-Gutiérrez, 2001).

The differential patterns of brain activation obtained by the pleasant exciting emotions induced by Mahler, minus pleasant relaxing emotions elicited by Bach involved the right inferior parietal lobule (BA40) and parahippocampal regions, more extensive and anterior on the right side. The rest of the activated regions were also differentially activated by music and noise or by pleasant and unpleasant feelings (Table 2 and Fig. 4A).

Pleasant relaxing emotions (Bach) minus pleasant exciting emotions (Mahler) induced higher coherent activity between the P3 electrode and F3, F7, and Fz at 13 Hz. Inverse subtractions induced higher coherent activity than pleasant relaxing emotions (Bach) between T3 and Fp1 at 11 and 15 Hz. The rest of the combinations were also significant between

music and noise or between pleasant unpleasant feelings (Table 3 and Fig. 4B).

3.5. fMRI and EEG coherent activity differences between music and noise

In order to provide a further control of the changes related to the emotional effects of music, brain activity during the three pieces was averaged and compared to the averaged three periods of noise (Table 2 and Fig. 5). By evaluating all three musical stimuli together against the noise stimulus the distinct emotional effects of the three musical pieces were cancelled and only very general aspects of musical organization were preserved in the analysis. Thus, the comparison between music and noise would reveal broad perceptual and cognitive musical processing that was common to the three pieces but distinct from the homogeneous auditory stimulation of the random noise.

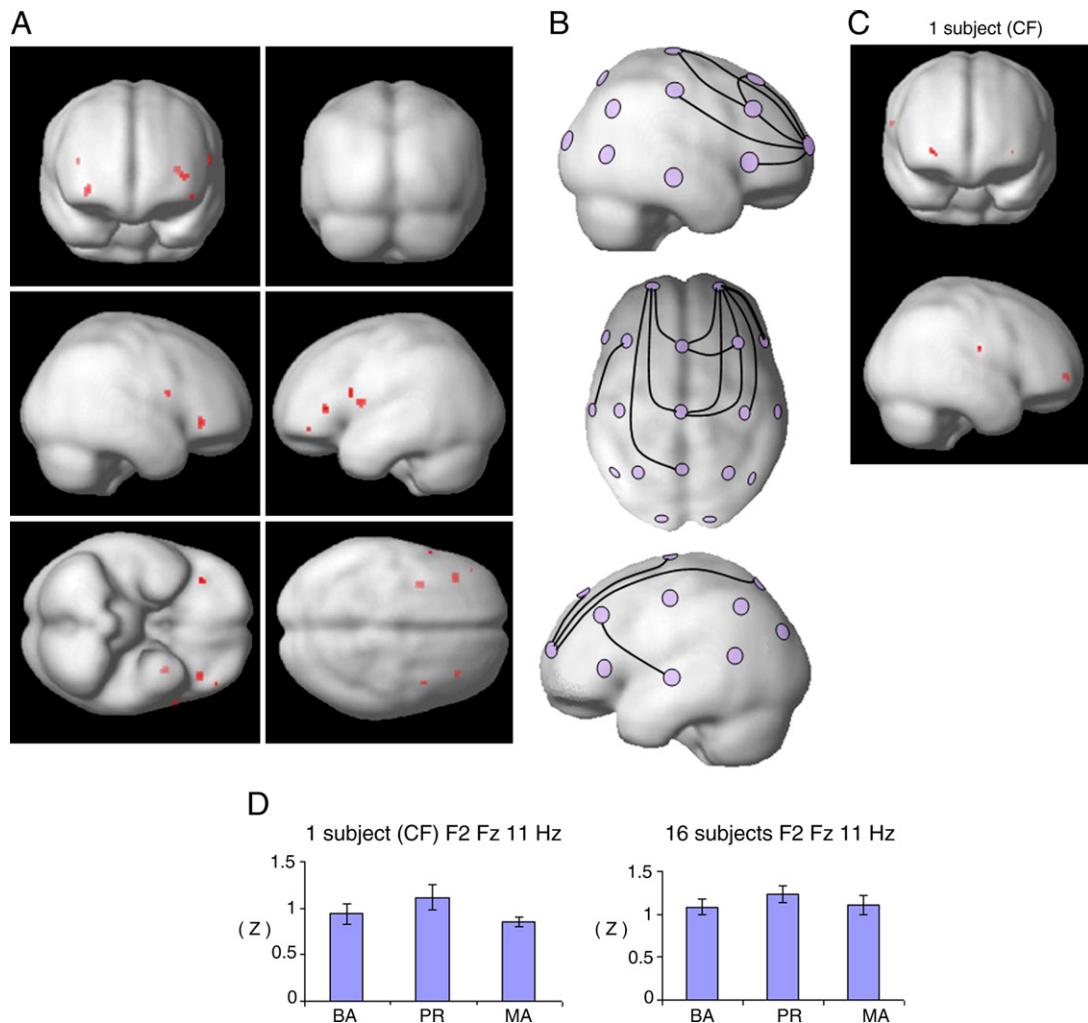


Fig. 3. fMRI and coherent EEG images during unpleasant music emotion (Prodromidès vs. Bach and/or Mahler) superimposed on a three-dimensional average brain template. A: averaged fMRI activations across subjects demonstrating areas in which the activity surpasses the threshold of $p < 0.05$ (corrected). Red colour indicates higher activation sites with unpleasant as compared to pleasant music emotions (see Table 2 for corresponding coordinates and areas). Left column: anterior, right, and inferior views. Right column: posterior, left, and superior views. B: Lines connecting electrodes indicate significantly higher coherent EEG activity with unpleasant than pleasant music (see Table 3 for corresponding frequencies). C: Single subject fMRI illustration of frontal and right hemisphere activation. D: EEG correlation profile similarity in full sample (right) and a single subject (left). Brain surface location of the electrodes used the distribution of Okamoto (Okamoto et al., 2004) on the average brain image by Evans (Evans et al., 1993).

The three pieces of music analyzed together against all three sections of noise modified brain activity in a different way than that related to emotional states. Slightly asymmetric bilateral activation with music as compared to noise was revealed by fMRI (Table 2 and Fig. 5A). The activated areas were the superior temporal gyrus near the primary auditory cortex (left BA41 and right BA42) and the right superior temporal gyrus over the auditory association cortex (BA22). Besides from bilateral primary auditory activation, in the left hemisphere the temporal pole (BA38) the inferior frontal gyrus (BA47) and frontopolar area (BA9) are activated. The right hypothalamic areas were also activated.

Coherent EEG activity increased with music average as compared to noise average (Table 3 and Fig. 5B) in two bilateral nodal points (T3 and T4, O1 and O2) and decreased between anterior and posterior electrodes. These points generally correspond with the primary auditory, prefrontal, and Broca areas that were found to be activated in fMRI.

4. Discussion

In the present study brain correlates of some emotional states evoked by three excerpts of instrumental music were analyzed. The simultaneous application of standardized subjective evaluations, fMRI, and analysis of EEG coherent activity offered adequate means to reveal both brain sites (fMRI) and functional relations (EEG coherent activity) underlying some musical emotional experiences. Listening without any cognitive task except paying attention to the music engaged a widespread and diverse activation of brain sites and networks. Different brain systems were involved in the perceptual and affective processing of the selected pieces, and particularly in the processing of the positive and negative musical emotions.

Even though multiple musical factors such as spectrum, notes, intensity, instruments, tonal norms, and other expressive features are stimuli that elicit a complex differential activation of brain patterns (Peretz and Zatorre, 2005), these effects were

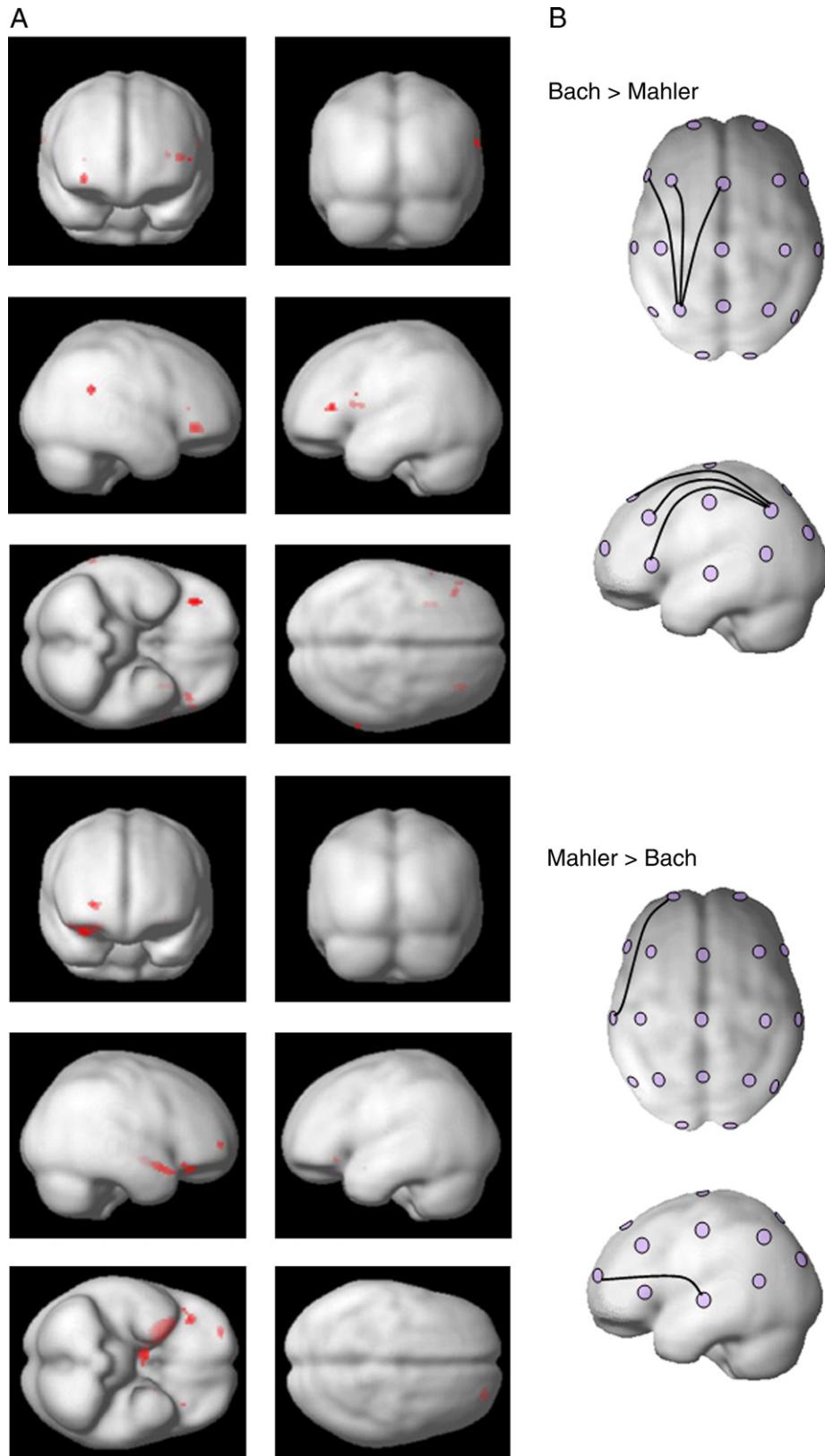


Fig. 4. fMRI and coherent EEG images during emotional “activation” (Bach—calmness vs. Mahler—excitement) superimposed on a three-dimensional average brain template. A: Averaged fMRI activations across subjects demonstrating areas in which the activity surpasses the threshold of $p < 0.05$ (corrected). Red colour indicates higher activation sites with calmness (Upper part: Bach > Mahler) and excitement (Lower part: Mahler > Bach) (see Table 2 for corresponding coordinates and areas). Left column: anterior, right, and inferior views. Right column: posterior, left, and superior views. B: Lines connecting electrodes indicate significantly higher coherent EEG activity with calmness (upper part: Bach > Mahler) and excitement (lower part Mahler > Bach) (See Table 3 for corresponding frequencies). Brain surface location of the electrodes used the distribution of Okamoto (Okamoto et al., 2004) on the average brain image by Evans (Evans et al., 1993).

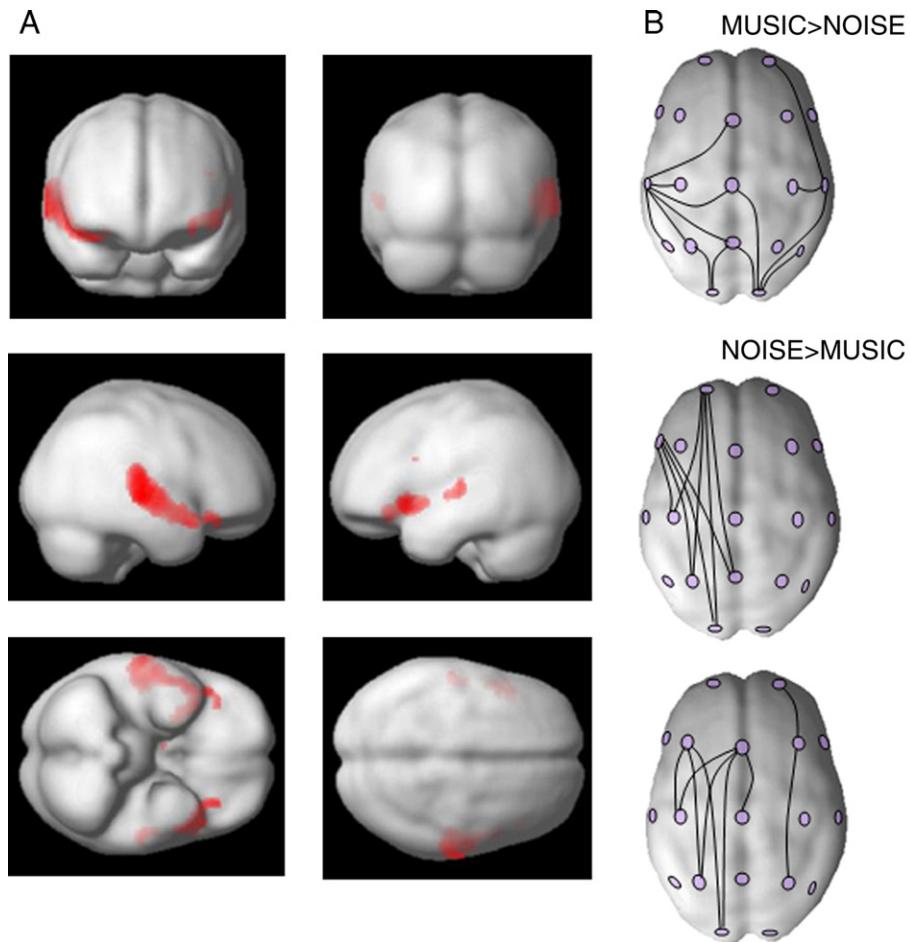


Fig. 5. fMRI and coherent EEG images of prevailing music feature parameters (all music stimuli minus noise) superimposed on a three-dimensional average brain template. A: averaged fMRI activations across subjects demonstrating areas in which the activity surpasses the threshold of $p < 0.05$ (corrected). Red colour indicates higher activation sites with music as compared to noise (see Table 2 for corresponding coordinates and areas). Left column: anterior, right, and inferior views. Right column: posterior, left, and superior views. B: Lines connecting electrodes indicate significant differences in coherent EEG activity between music and noise (see Table 3 for corresponding frequencies). Brain surface location of the electrodes used the distribution of Okamoto (Okamoto et al., 2004) on the average brain image by Evans (Evans et al., 1993).

not the purpose of this study, but the overall and average emotional effects reported after the still and attentive listening of unfamiliar music masterpieces. The strategy of analyzing together music compositions (Bach and Mahler) widely differing in musical elements but evoking similarly enjoyable effects is a strict control of the intervening musical features.

The choice of two pleasant pieces with different structure (Bach and Mahler), but only one unpleasant piece (Prodromidès) leaves the factor of musical features somewhat out of balance and prevents a definitive interpretation of the role of musical structure and dynamics in the activation domain. Nevertheless, the purpose to analyze positive and negative musical emotions was attained since the activated brain regions diverge between them. The comparison of pleasant and unpleasant musical emotions among themselves and with a neutral noise of similar intensity supports the relevance of the experimental approach, particularly since there is no truly emotional neutral music to be used as a suitable control. A validated subjective evaluation test using multiple feeling terms, and a Principal Component Analysis of such assessment,

clustered two opposite emotional poles (pleasant and unpleasant feelings), and an activation profile. The level of attention was reported to be similar to the three pieces. Once this objective was properly accomplished, it was justified to compare the metabolic and electrical brain correlates to each one of these three significant affective factors.

Subjective evaluations of the three musical stimuli were similar to those previously obtained by Ramos et al. (1996) and Flores-Gutiérrez (2001). The masterpiece selection was based on these studies where the distinction between emotional terms was based on meticulous tests. These results justified four types of analyses: (1) pleasant musical emotion (Mahler and Bach vs. Prodromidès), (2) unpleasant musical emotion (Prodromidès vs. Bach and Mahler), (3) musical “activation” in terms of excitement (Mahler vs. Bach) or calmness (Bach vs. Mahler), and (4) general musical structure features not including specific emotions (Bach+Mahler+Prodromidès vs. noise). Even though the sample size for fMRI ($N=6$) may be considered insufficient, the high level of significance required in the average and common group results abated possible idiosyncratic or

individual effects. Nevertheless the limited number of subjects makes these results preliminary and the outcome somewhat speculative before confirmation occurs.

While some of the fMRI data seem to match the EEG coherence data, there are other instances where there is no correspondence between the respective areas of activation. Even though a full correspondence between the two sets of results should not be expected because they measure different physiological processes, it seems sound to assign special relevance to the areas where metabolic and electric matching occurs. Both fMRI and EEG coherence approaches identified divergent brain networks for positive and negative music affective valence. A left cortical system involved with pleasant music feelings included the posterior temporal–parietal, occipital, and middle prefrontal regions. A coherent activity in upper alpha frequencies took place between most left hemisphere electrodes with a nodal focus in the temporo-parietal and occipital regions indicating a functional coupling among some of the activated regions identified by fMRI.

Left hemisphere activation with pleasant musical feelings is consistent with reported activation of left fronto-temporal areas with pleasant feelings using DC potentials (Altenmüller et al., 2002), event related potentials (Koelsch and Mulder, 2002), PET (Blood et al., 1999), and fMRI (Herrington et al., 2005). The participation of the middle frontal cortex seems to be involved in the general processing of emotion, since it is activated by both happiness and sadness (Khalfa et al., 2005). While the left parietal lobe is activated by rhythm processing (Sakai et al., 1999; Parsons, 2001) and musical phrasing (Besson and Schön, 2001), both frontal and parietal sites are important for time perception (Harrington et al., 1998). The changes in upper alpha coherent activity are compatible both with their role in complex perceptual processes (Basar et al., 2001) and with a possible binding function (Nunez et al., 2001). Furthermore, a synchronization of neural oscillations between prefrontal and posterior association areas has been reported to facilitate the integration of perception and working memory (Sarnthein et al., 1998) and this would be necessary for the preservation of the musical features that make musical perception possible. Even though the right hypothalamus activation is small and requires further confirmation, it may relate to the autonomous effects of emotion (Damasio et al., 2000; Blood and Zatorre, 2001). Two recent papers (Blood and Zatorre, 2001; Brown et al., 2004) have shown strong activation in the nucleus accumbens when subjects were listening to emotionally delightful musical excerpts. The lack of activation in the reward system after the contrast of positive and negative musical excerpts in the present results was probably due to the fact that the stimuli were not chosen for their intensity and the subjects accordingly reported only moderate pleasant feelings.

The activation of the left primary auditory cortex by pleasant music is an unexpected finding of great consequence because it would imply that musical emotion is processed upon arrival of the stimulus at the earliest cortical location, traditionally considered to discriminate only for fundamental sensory features. Even though, as expected, all three music stimuli activated the superior temporal gyrus in both hemispheres, only

pleasant musical emotions involved the left gyrus and only unpleasant ones the right gyrus. It is feasible that the recognition of particular perceptual music features is prone to induce pleasant emotions. Pleasant affective musical processing may involve auditory areas in the dominant hemisphere providing some musical stimuli with a primary positive valence while unpleasant music involves the right auditory areas contributing to an initial attribution of negative emotion. Other studies have found a right ear (left hemisphere) advantage for pleasantness ratings of tonal and atonal melodies (Gagnon and Peretz, 2000). Specific feelings elicited by music require the extraction of a meaning involving subsequent cortical locations. The activation and functional coupling among posterior temporal, inferior parietal and prefrontal regions seem to be needed to accomplish this task.

The left lateralization of pleasant emotion by music may be related to structural and functional asymmetries of the temporal lobe (Penhune et al., 1996), providing a substrate for temporal processing and perhaps for coherent activity. Temporal sequencing is needed to comprehend musical or language phrases and left hemisphere superiority has been established for the comprehension of temporal sounds (Griffiths et al., 1998; Liégeois-Chauvel et al., 1999; Ioannides et al., 2003), auditory sequences (Binder et al., 1996; Besson and Schön, 2001), interval regularities (Samson et al., 2001), and complex melodic strings (Platel et al., 1997; Patel and Balaban, 2000).

In contrast to pleasant musical feelings, unpleasant emotions evoked by dissonant and athematic music involved the activation of right superior frontopolar region, left middle frontal cortex, a slightly asymmetrical activation of the inferior frontal gyrus and insula, and right auditory area (BA42 Mahler vs. Prodromidiès). Unpleasant emotions were associated with an increased coherent activity among both prefrontal and midline electrodes towards the right frontal and left temporal regions disrupting coherent activity with posterior regions in the left hemisphere. Activation areas involving right cortical regions were found only for unpleasant emotions both with fMRI and EEG. The regions involved in unpleasant feelings, namely medial and orbitofrontal cortex, cingulum, and insula, are important constituents of the paralimbic system. The anterior cingulate is important for attention and for the evaluation of conflicting demands, while the dorsal part is involved in cognitive requirements (Bush et al., 2000; Allman et al., 2001). The stronger activation of the insula in the negative emotional condition is in agreement with the involvement of this region in emotional arousal through the mapping and regulating of body signals (Baumgartner et al., 2006). The finding that the calming positive musical excerpt compared with the arousing positive excerpt also shows activation in the insula is not surprising since pleasant musical feelings have been correlated with activation in this region (Blood and Zatorre, 2001; Brown et al., 2004; Koelsch et al., 2006).

The predominance of left hemisphere activation with pleasant musical feelings and right activation with unpleasant ones is consistent with findings that relate right frontal activation with negative affect and left frontal activation with positive affect (Davidson, 1992). This result is consistent with

right hemisphere predominance for dealing with novel cognitive situations and the left hemisphere for predictable representations and strategies, such as language (Podell et al., 2001). Bach's and Mahler's are masterpieces that follow melody and harmony rules leading to a fulfilment of expectations. In contrast, the piece by Prodromidès breaks classical musical grammar rules probably demanding the participation of limbic and right hemisphere regions in the search for emotional comprehension. Nevertheless, a valence lateralization cannot be considered definitive since Khalfa et al. (2005) have reported left activation of BA9 and BA10 with both happy and fearful stimuli.

In addition to the bilateral auditory sensory areas, brain regions involved in working memory, attention, and language processing were recruited in non-affective perceptual responses as determined by comparing all three musical pieces against noise. Musical stimuli activate areas involved in syntactic and semantic language processing (Samson et al., 2001; Besson and Schön, 2001; Koelsch et al., 2002), working memory (Zatorre et al., 1994), perceptual integration, and search for meaning (Patterson et al., 2002; Janata et al., 2002; Platel et al., 2003). Musical sequences activate overlapping brain regions involved both in language (Koelsch et al., 2002, 2004) and in music appraisal (Besson and Schön, 2001; Samson et al., 2001). Music is a highly complex and precisely organized stimulus requiring different brain modules and systems involved in distinct cognitive tasks including the meaning extraction of a nonverbal message (Mesulam, 1998; Michel et al., 2001; Newman, 1997). Not only the similarities between music and language have justified the notion of *music semantics* (Meyer, 1956; Brown, 2001) but Damasio (1989) and Mesulam (1998) consider the attribution of meaning to a stimulus of any modality as properly semantic.

The combined Principal Component Analysis of validated reports, brain fMRI and coherent EEG correlates of emotional reactions to music analyzed in non-musicians during the listening of unfamiliar instrumental masterpieces is an effective approach to detect a predominant left hemisphere activation with pleasant music emotions and right hemisphere activation with negative emotions.

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References

- Allman, J.M., Hakeem, A., Erwin, J.M., Nimchinsky, E., Hof, P., 2001. The anterior cingulated cortex: the evolution of an interface between emotion and cognition. Ann. N.Y. Acad. Sci. 935, 107–117.
- Altenmüller, E.O., Shurman, K., Lim, V.K., Parlitz, D., 2002. Hits to the left, flops to the right: different emotions during listening to music are reflected in cortical lateralization patterns. *Neuropsychologia* 40, 2242–2256.
- Balkwill, L., Thompson, W.F., 1999. A cross-cultural investigation of the perception of emotion in music: psychophysical and cultural cues. *Music Percept.* 17, 43–64.
- Basar, E., Basar-Eroglu, C., Karakas, S., Schürmann, M., 2001. Gamma, alpha, delta and theta oscillations govern cognitive processes. *Int. J. Psychophysiol.* 39, 241–248.
- Baumgartner, T., Lutz, K., Schmidt, C.F., Jäncke, L., 2006. The emotional power of music: how music enhances the feeling of affective pictures. *Brain Res.* 1075 (1), 151–164.
- Besson, M., Schön, D., 2001. Comparison between language and music. *Ann. N.Y. Acad. Sci.* 930, 232–258.
- Bhattacharya, J., Petsche, H., Pereda, E., 2001. Long-range synchrony in the gamma band: role in music perception. *J. Neurosci.* 21, 6329–6337.
- Binder, J.R., Frost, J.A., Hammeke, T.A., Rao, S.M., Cox, R.W., 1996. Function of the left planum temporale in auditory and linguistic processing. *Brain* 119, 1239–1247.
- Blood, A.J., Zatorre, R.J., 2001. Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion. *Proc. Natl. Acad. Sci. U.S.A.* 98, 11818–11823.
- Blood, A.J., Zatorre, R.J., Bermudez, P., Evans, A.C., 1999. Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nat. Neurosci.* 2, 382–387.
- Brown, S., 2001. Are music and language homologues? *Ann. N.Y. Acad. Sci.* 930, 372–374.
- Brown, S., Martínez, M.J., Parsons, L.M., 2004. Passive music listening spontaneously engages limbic and paralimbic systems. *NeuroReport* 15, 2033–2037.
- Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn. Sci.* 4, 215–222.
- Corsi-Cabrera, M., Guevara, M.A., del Río-Portilla, Y., Arce, C., Villanueva-Hernández, Y., 2000. EEG bands during wakefulness, slow-wave and paradoxical sleep as a result of principal component analysis in man. *Sleep* 23, 738–744.
- Damasio, A.R., 1989. Time-locked multiregional retroactivation: a systems-level proposal for the neural substrates of recall and cognition. *Cognition* 33, 25–62.
- Damasio, A.R., Grabowski, T.J., Bechara, A., Damasio, H., Ponto, L.L.B., Parvizi, J., Hichwa, R.D., 2000. Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat. Neurosci.* 3, 1049–1056.
- Davidson, R.J., 1992. Anterior cerebral asymmetry and the nature of emotion. *Brain Cogn.* 20, 125–151.
- Díaz, J.L., Flores-Gutiérrez, E., 2001. La estructura de la emoción humana: un modelo cromático del sistema afectivo. *Salud Ment.* 24 (4), 20–35.
- Evans, A.C., Collins, D.L., Mills, S.R., Brown, E.D., Kelly, R.L., Peters, T.M., 1993. 3D statistical neuroanatomical models from 305 MRI volumes. Proceedings of IEEE-Nuclear Science Symposium and Medical Imaging Conference, pp. 1813–1817.
- Flores-Gutiérrez, E.O., 2001. La respuesta emocional a la música: atribución de términos de la emoción a segmentos musicales. Thesis for Master in Neurobiology. México: Universidad Nacional Autónoma de México.
- Friston, K.J., Tononi, G., Reeke Jr., G.N., Sporns, O., Edelman, G.M., 1994. Value-dependent selection in the brain: simulation in a synthetic neural model. *Neuroscience* 59, 229–243.
- Friston, K.J., Holmes, A.P., Poline, J.B., Grasby, P.J., Williams, S.C., Frackowiak, R.S., Turner, R., 1995. Analysis of fMRI time-series revisited. *NeuroImage* 2, 45–53.
- Gagnon, L., Peretz, I., 2000. Laterality effects in processing tonal and atonal melodies with affective and nonaffective task instructions. *Brain Cogn.* 43, 206–210.
- GRASS-GAMMA, 2005. Version 4.4. Grass Technologies. EEG Research Data Acquisition and Analysis System. Information: <http://www.grasstechnologies.com/products/researchsoft/gamma1.html>.
- Griffiths, T.D., Büchel, C., Frackowiak, R.S.J., Patterson, R.D., 1998. Analysis of temporal structure in sound by the brain. *Nat. Neurosci.* 1, 422–427.
- Guevara, M.A., Ramos, J., Zarabozo, D., Corsi-Cabrera, M., 2003. POTENCOR: a program to calculate power and correlation spectra of EEG signals.

- Comput. Methods Programs Biomed. 72, 241–250 (Available upon request: mguevara@cencar.udg.mx).
- Guilford, J.P., Fruchter, B., 1978. Fundamental Statistics in Psychology and Education. McGrawHill, México.
- Halpern, A.R., Zatorre, R.J., Bouffard, M., Johnson, A., 2004. Behavioral and neural correlates of perceived and imagined musical timbre. *Neuropsychologia* 42 (9), 1281–1292.
- Harrington, D.L., Haaland, K.Y., Knight, R.T., 1998. Cortical networks underlying mechanisms of time perception. *J. Neurosci.* 18, 1085–1095.
- Herrington, J.D., Mohanty, A., Koven, N.S., Fisher, J.E., Stewart, J.L., Banich, M.T., Webb, A.G., Miller, G.A., Heller, W., 2005. Emotion-modulated performance and activity in left dorsolateral prefrontal cortex. *Emotion* 5 (2), 200–700.
- Hevner, K., 1936. Experimental studies of the elements of expression in music. *Am. J. Psychol.* 48, 246–268.
- Huron, D., 2001. Is music an evolutionary adaptation? *Ann. N.Y. Acad. Sci.* 930, 43–61.
- Ioannides, A.A., Popescu, M., Otsuka, A., Bezerianos, A., Liu, L., 2003. Magnetoencephalographic evidence of the interhemispheric asymmetry in echoic memory lifetime and its dependence on handedness and gender. *NeuroImage* 19, 1061–1075.
- Janata, P., Birk, J.L., vHorn, J.D., Leman, M., Tillman, B., Bharucha, J.J., 2002. The cortical topography of tonal structures underlying western music. *Science* 298, 2167–2170.
- Jolliffe, I.T., 1986. Principal Component Analysis. Springer-Verlag, New York.
- Khalfa, S., Schon, D., Anton, J.L., Liegeois-Chauvel, C., 2005. Brain regions involved in the recognition of happiness and sadness in music. *NeuroReport* 16, 1981–1984.
- Klimesch, W., 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res. Rev.* 29, 169–195.
- Koelsch, S., Mulder, J., 2002. Electric brain responses to inappropriate harmonies during listening to expressive music. *Clin. Neurophysiol.* 113, 862–869.
- Koelsch, S., Gunter, T.C., Crimon, D., Zysset, S., Lohmann, G., Friederici, A.D., 2002. Bach speaks: a critical cortical “language-network” serves the processing of music. *NeuroImage* 17, 956–966.
- Koelsch, S., Kasper, E., Gunter, T.C., Sammler, D., Schulze, K., Friederici, A.D., 2004. Music, language, and meaning: brain signatures of semantic processing. *Nat. Neurosci.* 7, 302–307.
- Koelsch, S., Fritz, T., v Cramon, D.Y., Muller, K., Friederici, A.D., 2006. Investigating emotion with music: an fMRI study. *Hum. Brain Mapp.* 27, 239–250.
- Krumhansl, C.L., 2003. Dissecting the perceptual components of music. *Ann. N.Y. Acad. Sci.* 999, 103–105.
- Lancaster, J.L., Woldorff, M.G., Parsons, L.M., Liotti, M., Freitas, C.S., Rainey, L., Kochunov, P.V., Nickerson, D., Mikiten, S.A., Fox, P.T., 2000. Automated Talairach Atlas labels for functional brain mapping. *Hum. Brain Mapp.* 10, 120–131.
- Liégeois-Chauvel, C., De Graaf, J.B., Laguitton, V., Chauvel, P., 1999. Specialization of left auditory cortex for speech perception in man depends on temporal coding. *Cereb. Cortex* 9, 484–496.
- Merica, H., Fortune, R.D., 2005. Spectral power time-courses of human sleep reveal a striking discontinuity at 18 Hz parking the division between NREM-specific and Wake/REM-specific fast frequency activity. *Cereb. Cortex* 15, 877–884.
- Mesulam, M.M., 1998. From sensation to cognition. *Brain* 121, 2–52.
- Meyer, L., 1956. Emotion and Meaning in Music. The University of Chicago Press, Chicago, Ill.
- Michel, C.M., Thut, G., Morand, S., Khateb, A., Pegna, A.J., Gravel de Peralta, R., Gonzalez, S., Seeck, M., Landis, T., 2001. Electric source imaging of human brain functions. *Brain Res. Brain Res. Rev.* 36, 108–118.
- Mullholland, T.B., 1995. Human EEG, behavioral stillness and biofeedback. *Int. J. Psychophysiol.* 19, 263–279.
- Newman, J., 1997. Putting the puzzle together, Part I: towards a general theory of the neural correlates of consciousness. *J. Conscious. Stud.* 4, 47–66.
- Niedermeyer, E., 1998. The normal EEG of the waking adult, In: Niedermeyer, E., Lopes da Silva, F. (Eds.), *Electroencephalography: Basic Principles, Clinical Applications and Related Fields*, 4th ed. Lippincot Williams and Wilkins, Baltimore, Maryland, U.S.A, pp. 149–173.
- Nunez, P.L., Wingier, B.M., Silberstein, R.B., 2001. Spatial-temporal structures of human alpha rhythms: theory, microcurrent sources, multiscale measurements and global binding of local networks. *Hum. Brain Mapp.* 13, 125–164.
- Ogata, S., 1995. Human EEG responses to classical music and simulated white noise: effects of a musical loudness component on consciousness. *Percept. Mot. Skills* 80, 79–90.
- Okamoto, M., Dan, H., Sakamoto, K., Tadeo, K., Shimizu, K., Cono, S., Oda, I., Isobe, S., Suzuki, T., Johyama, K., Dan, I., 2004. Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10–20 system oriented for transcranial functional brain mapping. *NeuroImage* 21, 99–111.
- Parsons, L.W., 2001. Exploring the functional neuroanatomy of music performance, perception, and comprehension. *Ann. N.Y. Acad. Sci.* 930, 211–230.
- Patel, A.D., Balaban, E., 2000. Temporal patterns of human cortical activity reflect tone sequence structure. *Nature* 404, 80–84.
- Patterson, R.D., Uppenkamp, S., Johnsrude, I.S., Griffiths, T., 2002. The processing of temporal pitch and melody information in auditory cortex. *Neuron* 36, 767–776.
- Penhune, V.B., Zatorre, R.J., MacDonald, J.D., Evans, A.C., 1996. Interhemispheric anatomical differences in human primary auditory cortex: probabilistic mapping and volume measurement from magnetic resonance scans. *Cereb. Cortex* 6, 661–672.
- Peretz, I., Zatorre, R., 2005. Brain organization for music processing. *Annu. Rev. Psychol.* 56, 89–114.
- Petsche, H., Etlinger, S.C., 1998. EEG and Thinking: Power and Coherence Analysis of Cognitive Processes. Austrian Academy of Sciences, Vienna, pp. 81–126.
- Platel, H., Price, C., Wise, J.C., Lambert, R., Frackowiak, R., Lechevalier, B., Eustache, F., 1997. The structural components of music perception. *Brain* 120, 229–243.
- Platel, H., Baron, J.C., Desgranges, B., Bernard, F., Eustache, F., 2003. Semantic and episodic memory of music are subserved by distinct neural networks. *NeuroImage* 20, 244–256.
- Podell, K., Lovell, M., Goldberg, E., 2001. Lateralization of frontal lobe functions. In: Salloway, S.P., Malloy, P.F., Duffy, J.D. (Eds.), *The Frontal Lobes and Neuropsychiatric Illness*. American Psychiatric Publishing, London, pp. 83–99.
- Ramos, J., Corsi-Cabrera, M., 1989. Does brain electrical activity react to music? *Int. J. Neurosci.* 47, 351–357.
- Ramos, J., Guevara, M.A., Martínez, A., Arce, C., Del Rio, Y., Amescua, C., Corsi-Cabrera, M., 1996. Evaluación de los estados afectivos provocados por la música. *Rev. Mex. Psicol.* 13, 131–145.
- Rorden, Ch., 2000. MRIcro. Software that complement SPM allows analyse MRI, fMRI and PET images. University of South Carolina, Columbia SC 29208, USA. Available from: <http://www.sph.sc.edu/comd/rorden/micro.html>.
- Sakai, K., Hikosaka, O., Miyachi, S., Ryousuke, T., Tamada, T., Iwata, K.N., Nielsen, M., 1999. Neural representation of a rhythm depends on its interval ratio. *J. Neurosci.* 19, 10074–10081.
- Samson, S., Ehrlé, N., Baulac, M., 2001. Cerebral substrates for musical temporal processing. *Ann. N.Y. Acad. Sci.* 930, 166–178.
- Sarnthein, J., Petsche, H., Rappelsberger, P., Shaw, G.L., von Stein, A., 1998. Synchronization between prefrontal and posterior association cortex during human working memory. *Proc. Natl. Acad. Sci. U. S. A.* 95, 7092–7096.
- Schmidt, L.A., Trainor, L.J., 2001. Frontal brain electrical activity (EEG) distinguishes valence and intensity of musical emotions. *Cogn. Emot.* 15, 487–500.
- Singer, W., 1999. Neuronal synchrony: a versatile code for the definition of relations? *Neuron* 24, 49–65.
- Solis-Ortiz, S., Ramos, J., Arce, C., Guevara, M.A., Corsi-Cabrera, M., 1994. EEG oscillations during menstrual cycle. *Int. J. Neurosci.* 76, 279–292.
- SPM, 2006. Statistical Parametric Mapping (SPM) Analysis of Brain Imaging Data Sequences Software. Wellcome Department of Imaging

- Neuroscience, Institute of Neurology, UCL, London WC1N 3BG UK,
Available from: <http://www.fil.ion.ucl.ac.uk/spm/>.
- Thayer, R.E., Newman, J.R., McLain, T.M., 1994. The self regulation of mood: strategies for changing a bad mood, raising energy and reducing tension. *J. Pers. Soc. Psychol.* 67, 910–925.
- Wieser, H.G., Mazzola, G., 1986. Musical consonances and dissonances: are they distinguished independently by the right and left hippocampi? *Neuropsychologia* 24, 805–812.
- Zatorre, R.J., 2001. Neural specializations for tonal processing. *Ann. N.Y. Acad. Sci.* 930, 193–210.
- Zatorre, R., Evans, A., Meyer, E., 1994. Neural mechanisms underlying melodic perception and memory for pitch. *J. Neurosci.* 14, 1908–1919.